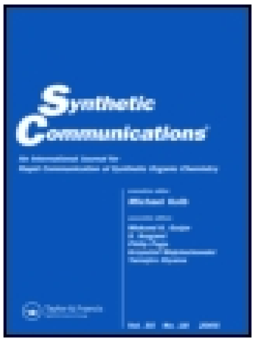

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Electrochemical Bromination of Cyclic and Acyclic Enes Using Biphasic Electrolysis

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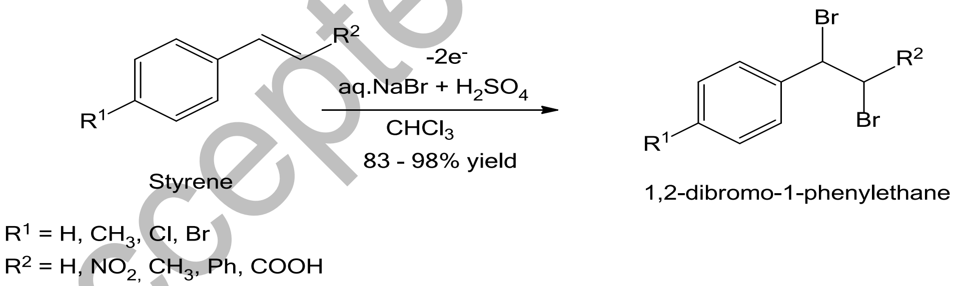
Supplemental data for this article can be accessed on the publisher's website.

Abstract

A simple method of electrochemical bromination of a series of cyclic and acyclic enes (styrene and substituted styrenes, stilbene, indene and cyclooctene) in biphasic water-chloroform mixture mediated by bromide/bromine redox system is reported. Aqueous 25% NaBr/ H_2SO_4 is used as the electrolyte. Regio and stereo selective dibromination of enes is achieved. Moderate to excellent yields of the product (83-98%) is obtained depending on the substrate. Electrolyte reuse has also been demonstrated successfully using HBr in the dibromination of styrene.



KEYWORDS: Cyclic and acyclic enes, Dibromide, Electrolytic oxidation, Biphasic media, Stereo-selectivity

INTRODUCTION

Vicinal dibromides are useful intermediates for the synthesis of pharmaceuticals, dyes, flame retardants, agro chemicals, additives, plasticizers and specialty chemicals. [1] GC analysis with element-selective plasma spectroscopic detection of the dibromo derivatives is a selective and sensitive method for alkenes determination in different complex matrixes. [2]

Classical bromination of enes is disadvantageous as it involves the use of elemental bromine [3] and further it generates hazardous HBr as byproduct. The use of *N*-bromoimide [4] is a better option as it does not produce HBr during bromination. However, these methods are expensive and generate organic waste during the reaction. Another drawback of these methods is low product yield and long reaction times.

Still oxidative bromination of alkenes with HBr-DMSO [5] and HBr-sodium nitrite [6] are being reported to effect dibromination.

Presently oxidative bromination is preferred as it avoids the use of volatile, hazardous bromine. This method requires a metal salt as bromine source, an oxidizing agent and a catalyst to carry out the transformation. [7-9] However, such oxidative brominations involve the use of heavier metals in stoichiometric amounts often resulting in poor yields due to unwanted side products.

Alternate brominating reagents such as pyridinium bromide-perbromide and quaternary ammonium tribromide are safer and easier to use but they are also produced using liquid bromine.[10,11] Bromodimethylsulfonium bromide, generated *in situ* by treating dimethyl sulfoxide with aqueous hydrobromic acid, is found to be a milder and more selective reagent for electrophilic aromatic bromination.

Of late, ionic liquids have been used as a reaction media for the bromination of alkenes with molecular bromine in presence of suitable solvents. [12-14] High polarity of ionic liquids makes them interesting media in which to conduct and investigate the selectivity and reactivity of ionic halogenation reactions. Also, ionic liquids avoid many of the problems associated with the volatility of common organic media and many ionic liquids can be separated easily from the products and/or catalysts and reused. Dibromination of alkenes in basic ionic liquids offered high yields of dibromo products with chemo and stereo selectivity and recycling of ionic liquids was rendered possible but however bromine was used as the brominating agent.[15]

Another approach to mediating the selectivity and reactivity of halogenations involves using trihalide anions XY_2^- (X,Y = Cl, Br, I) as the halogen reagent, and studies that combine trihalide ions and ionic liquids as the medium have been conducted. [16] Finally, the trihalide anion has been made a part of ionic liquid so that the solvent alone is an efficient halogenating material. For example, halogenations in salts of tetraalkylammonium and imidazolium trihalides have been used to examine the role of the cation and anion structures on the kinetics of the reactions, the stability of the reaction intermediates, and, thus, the reactivity and selectivity of the substrates.

The reactivity of electrogenerated bromine with cyclohexene has been reported [17] on a platinum micro electrode by linear sweep and cyclic voltammetry in acetonitrile as well as in 1-butyl-3-methylimidazoliumbis[(trifluoromethyl)sulfonyl]imide. Bulk electrolysis and NMR spectroscopy confirmed *trans*-1,2-dibromocyclohexane or *trans*-1-(*N*-acetylamino)-2-bromocyclohexane as the product depending on whether ionic liquid or acetonitrile was used as the media.

Torii et al reported the dibromides of 4-cyclohexene-1, 2-dicarboxylate and few acyclic olefins performed by electrolysis in MeCN-H_2O-NaBr-(Pt) system. Higher bromide concentration (> 1.5 M in acidic medium) was found to favour dibromide formation whereas lower concentrations of bromide favoured epoxide or bromohydrin formation. [18]

In spite of variety of methods available for the preparation of vicinal dibromides, many of them use expensive reagents and further, mixture of products are formed resulting in low yields of the desired product. The replacement of such reagents by a cheap, non-toxic, mild and selective reagent is desirable and represents an important goal in the context of clean synthesis.

In continuation of our interest on the halogen reactions, herein we report a very simply mild and efficient method for the synthesis of dibromide from olefins using aqueous NaBr with catalytic amount of H_2SO_4 in a high regio and stereo selective fashion. Environmental friendly electrochemical bromination of styrene and its derivatives are not reported so far.

The present work reports the electrochemical bromination of a variety of cyclic and acyclic enes including styrene and substituted styrenes, cyclooctene, indene and stilbene using biphasic media with bromide/bromine redox system. Handling of hazardous liquid bromine, used in conventional bromination, is avoided in the present work. Both sulphuric acid-NaBr and HBr-NaBr have been used as the aqueous electrolyte.

In biphasic electrolysis, the reactive species formed by the electrolytic oxidation of a halide ion in the aqueous phase can be taken continuously into the organic phase and then reacted with the substrate to give regioselectivity to the products. Biphasic electrolysis has a distinct advantage over conventional homogenous electrolysis in practical electro-organic synthesis. [19-22] In this present biphasic electrolysis process the extraction of product from the reaction mixture by an organic solvent is not necessary as the product concentration increases in the organic phase while the electrolysis proceeds. After completion of electrolysis the product containing organic phase can be separated by simple phase separation and the aqueous electrolyte can be reused which an important aspect is considered during the reaction scale up as this makes the process economical. This has been attempted with the use of HBr-NaBr as the electrolyte. Hence minimizing the use of organic solvents and reagents are the advantages of this green electro synthesis.

RESULTS AND DISCUSSION

The results on the electrochemical bromination of cyclic and acyclic enes are shown in Table 1 and Figure 1. It is observed that when the benzene ring of styrene is substituted with mild electron donating or electron withdrawing groups, the bromination proceeded smoothly (entry 2-4, Table 1) to yield 83-98% of the vicinal dibromide. However, when the alkene part of styrene had stronger +I (-CH_3) or –I (-NO_2) substituents, lesser yields of dibromides were obtained. Similarly in the case of o-chloro styrene, lower yield obtained could be due to steric effect of the o-chloro substituent. In the case of cinnamic acid, the erythro (54%) & threo (43%) forms of the dibromide were formed. The isomers were separated by crystallization with 50% ethanol. In the case of indene and cyclooctene, the dibromide is formed quantitatively.

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The current efficiencies are generally low as seen from Table 1 and this has also been reported by Torii [18] wherein 4 to 5 Faraday of charge was passed for dibromination of alkenes. The formation of HOBr and the possibility of bromate formation during bromine hydrolysis have also been reported. [23] These are also responsible for lowering of current efficiency. Further, distribution of bromine between the two phases also causes a part of bromine to be present in aqueous media.

The role of alkene geometry upon the addition of bromine was evident in the reactions of *cis* and *trans*-stilbene. While the *trans*-stilbene gave 87% of the meso dibromination product (anti addition) that melted at 232°C, *cis*- stilbene gave 95% of a mixture of threo dibrominated product (m.p: 110°C) and *trans*- stilbene oxide (m.p: 66°C) in equal amounts (Figure 2). Also, dibromination of *cis*- stilbene was more rapid than its *trans*-isomer. The reversibility of the first formed strained *cis*-bromonium ion is responsible for the formation of mixture of products from *cis*- stilbene. [24] The *trans*- stilbene gives higher yield of the dibromide than the *cis*- stilbene due to its lower molecular strain. The products were identified by comparison of their melting points and NMR spectra of the products obtained with that of the authentic samples.

The probable mechanism for the bromination of styrene (and olefins in general) is shown in Scheme 3 based on the literature. [25] The oxidation of bromide ion at the anode generates bromine which combines with Br^- to give Br_3^-. At the interface, Br_3^- which is in equilibrium with Br_2 and Br^- reacts with styrene to form the dibromide. Carbocation is formed by the reaction of styrene and Br^+ in the transition state and subsequently the cyclic bromonium ion is formed as the intermediate. The cyclic intermediate undergoes ring opening by the bromide ion as the nucleophile via S_N2 pathway to yield majority of the anti product. The stereochemistry of the product is confirmed by comparison with the previously reported data. [26]

The desirable approach of the present method is the environmentally friendly recycling procedure without any effluent generation. When 2 F/mole charge is passed to the aqueous NaBr solution, one equivalent of H_2 is generated at the vicinity of cathode and simultaneously one bromine molecule at the anode. After completion of electrolysis, addition of 2 equivalents of 47% HBr solution (w/v) [3.3g] to the aqueous phase and regenerates the original H_2SO_4 and bromide ion concentration which is depleted during the vicinal dibromide formation (equation 1-5, Figure 3).

The resulting aqueous phase was reused for electrolysis in the next cycle. By this method, the dibromination of styrene was successfully carried out for 4 cycles. So the electrolyte can be successfully reused for the dibromination reaction.

The present method offers several advantages over the existing methods.
The evaporation of bromine and chloroform is minimal during biphasic electrolysis as the aqueous layer is present over the chloroform layer and the reaction is carried out at 30^{o}C. The bromine generated at the aqueous phase was transferred to the organic phase where it was consumed instantaneously by the olefin present. After completion of electrolysis, the organic phase was separated carefully and after work up, the vicinal dibromide was isolated. In this process the formation and venting of hydrogen may be utilized in some other chemical process like hydrogenation of oils, Fuel cells or applied for oxygen reduction reactions.

Electrolyte Reuse:

The NaBr solution obtained from the above reaction mixture contained 2 equivalents (20mmol) lesser concentration of acid (due to passage of 2 F/mole of charge) and it was compensated by adding 3.3g [20 mmol] of 47% HBr solution (w/v) so as to have the same initial concentration of H_2SO_4 and bromide ion concentration. Subsequently, the resulting aqueous phase was taken back to the electrochemical cell and used as electrolyte to generate bromine. After completion of electrolysis with the same amount of styrene, the reaction mixture was worked up by the procedure as reported earlier and the isolated yield was determined. Similarly, the aqueous phase used as electrolyte for subsequent reuse maintained the same initial concentration of NaBr and H_2SO_4. For three such electrolyte reuses, the same yield of the product was isolated.

The product 1, 2-dibromo-1-phenyl ethane was obtained almost exclusively (Yield 98%) as shown in the Scheme 1. Styrene oxide was not formed as the product. The same procedure was extended to a series of substituted styrenes and also to other cyclic and acyclic enes to find the generality of the reaction.

CONCLUSIONS

A simple, efficient and eco friendly electrochemical dibromination of olefins is reported using aqueous 25% NaBr solution w/v containing H_2SO_4 with regio and stereo selectivity. Electrolyte reuse was also demonstrated successfully for the dibromination of styrene without much change in the product yield even after 3rd reuse. The advantages of the present method over the existing methods are i) handling the hazardous liquid bromine is avoided ii) cheap reagents are used iii) the effective utilization of cathodically generated OH^- by adding equimolar amount of HBr leads to zero effluent discharge to the environment iv) the products are easily separated from the reaction mixture by simple phase separation. V) the reaction conditions are mild and yield of the products are high and other possible by-products such as styrene epoxide, styrene bromohydrin are not observed. This process provides an alternative method based on aqueous phase reagents, where often much more expensive solutions are perused.

EXPERIMENTAL

Procedure For Synthesis Of 1,2 -Dibromo 1-Phenyl Ethane

A solution of styrene (1.04 g, 10mmol) in 25 ml $CHCl_3$ was taken in a beaker type glass jacketed undivided cell (100ml capacity) equipped with magnetic stirrer. To the above solution, 30 ml of 25% NaBr solution (w/v) containing 2.45g H_2SO_4 [25 mmol] was added. Two platinum foil electrodes of active area 7.5 cm^2 [3 cm × 2.5 cm] were placed carefully in the upper aqueous phase without touching the organic phase [Figure 4]. The inter electrode distance was maintained at 1 cm. The electrolysis was conducted galvanostatically at a current density of 40 mA/cm^2 and the charge corresponding to 2 Faraday was passed. The organic phase was stirred with a magnetic stirrer at a rate of 40 rpm in such a way that the organic phase does not touch the electrodes. During the course of reaction the cell voltage was measured to be 1.1 – 1.3 V. The electrolysis was continued till the reaction proceeded to completion.

The progress of the reaction was monitored by HPLC (Shimadzu) using Shimpack ODS-18 column (250 x 5 mm) as the stationary phase. The eluent consisted of 70:30 methanol: water. A flow rate of 1 ml per minute was employed. The samples were analyzed using a UV detector at a wave length of 254 nm. After the completion of electrolysis, the lower organic phase was carefully separated from the reaction mixture. The aqueous portion was saved for reuse after extraction with $CHCl_3$ (2 × 25ml). The combined organic phase was washed with water and dried over anhydrous sodium sulphate and distilled the solvent to get the product. .

Product Analytical Data - 1,2 -Dibromo 1-Phenyl Ethane

mp:71-73 ^{o}C; ^{1}H NMR (CDCl$_3$, 400 MHz) 7.44 – 7.32 (m, 3H) 5.15 (dd, J = 10.6, 5.4 Hz, 1H). 4.11-3.99 (m, 1H); ^{13}C NMR (CDCl$_{3,}$ 100 MHz) □ 138.2 , 129.2, 128.9 127.4, 50.9, 35.0.

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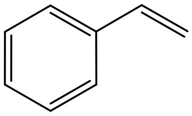
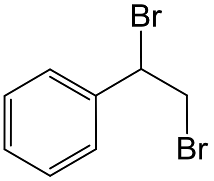
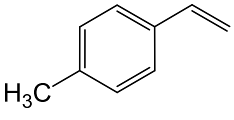
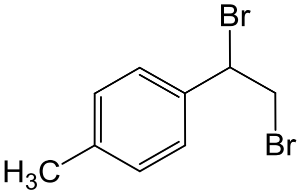
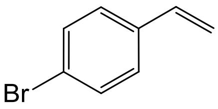
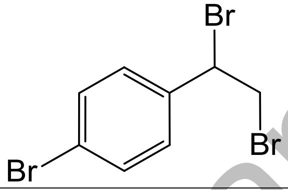
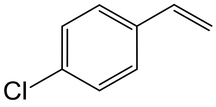
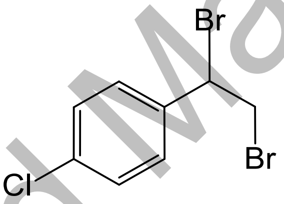
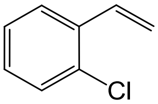
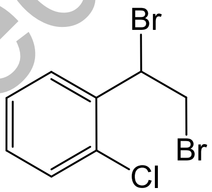
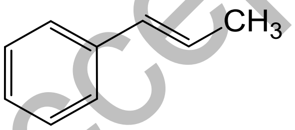
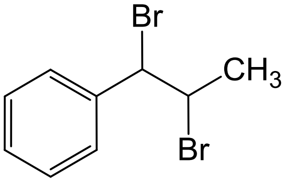
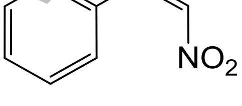
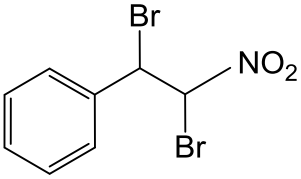
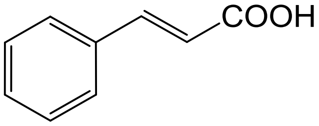
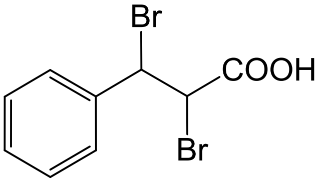
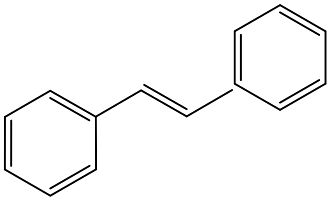
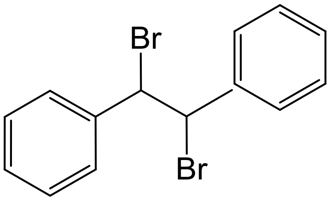
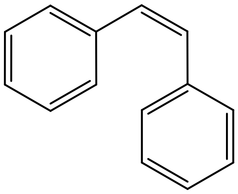
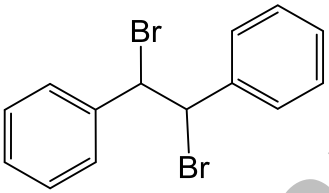
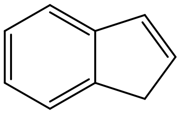
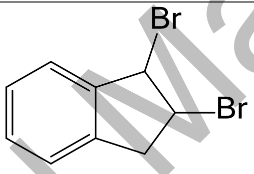
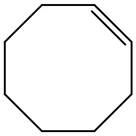
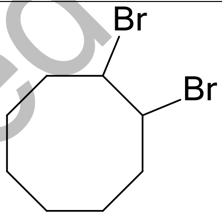
Table 1. Electrochemical bromination of styrenes by two-phase electrolysis

Sl No	Reactant	Product	Yield*(%)	Current efficiency**(%)
1			98	49
2			97	48
3			95	48
4			87	44
5			83	42
6			85	43
7			55	23

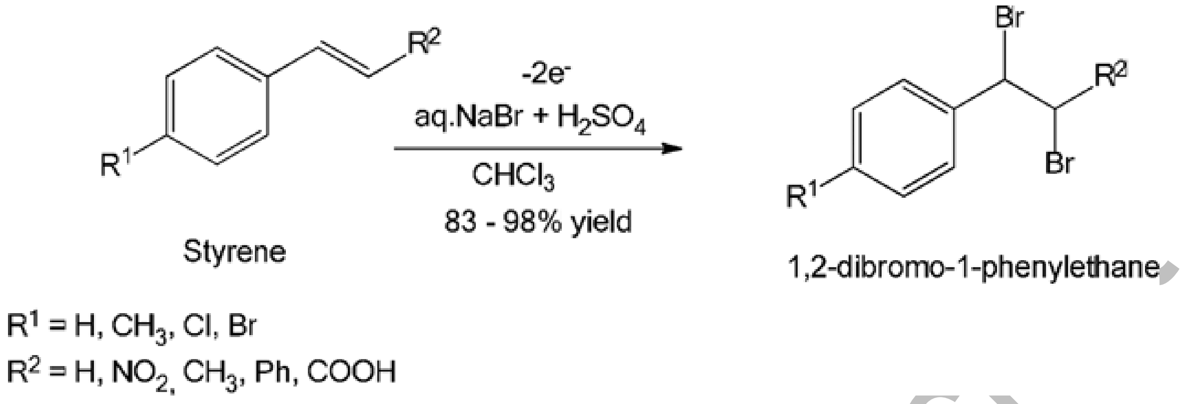
8			97	49
9			87	44
10			47***	24
11			95	48
12			83	42

* Yield based on the amount of product isolated

** Current efficiency based on the maximum yield of product obtained

*** 48% t-stilbene oxide is obtained along with 47% stilbene dibromide

Figure 1. Scheme for electrochemical bromination of styrene



R^1 = H, CH_3, Cl, Br

R^2 = H, NO_2, CH_3, Ph, COOH

Figure 2. Scheme for electrochemical bromination of *trans*-stilbene and *cis*-stilbene

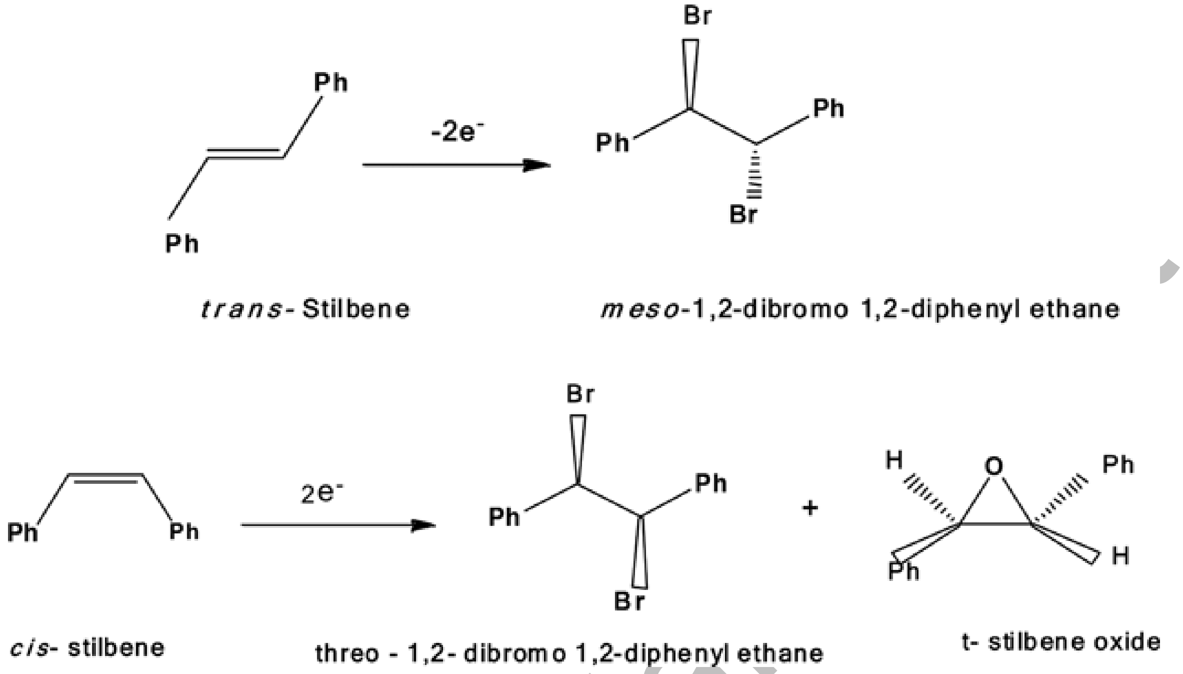


Figure 3. Scheme for bromination cycle showing regeneration of bromide

Aqueous phase

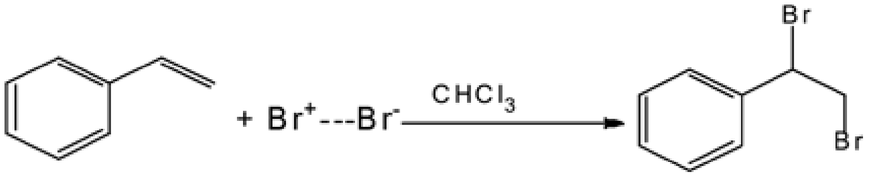
At the anode $2Br^- - 2e^- \longrightarrow Br_2$ (1)

At the cathode $H^+ + e^- \longrightarrow \frac{1}{2} H_2 \uparrow$ (2)

In solution $Br_2 + Br^- \rightleftarrows Br_3^-$ (3)

At the interphase $Br_3^- \rightleftarrows Br_2 + Br^-$ (4)

Organic phase



(5)

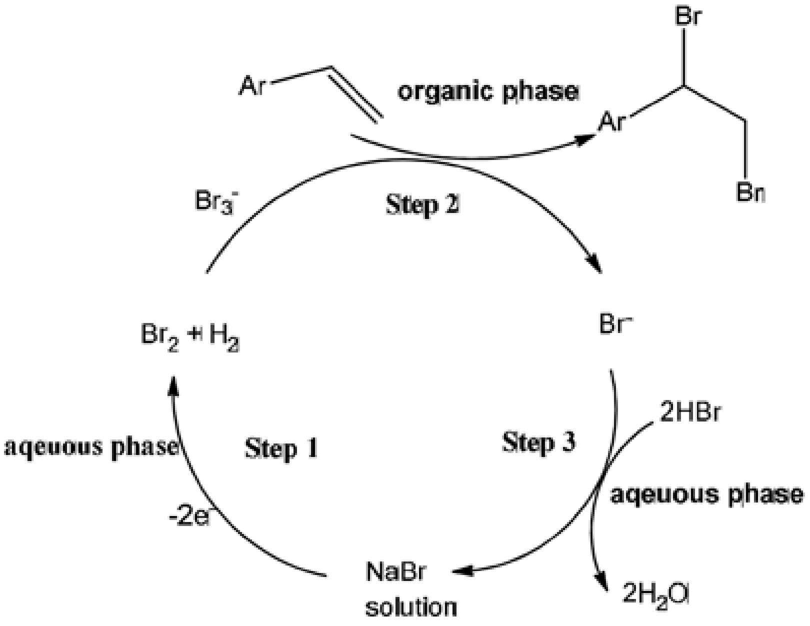


Figure 4. Electrochemical cell used for the bromination of cyclic and acyclic enes using biphasic electrolysis